

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
22 November 2001 (22.11.2001)

PCT

(10) International Publication Number  
**WO 01/88175 A1**

(51) International Patent Classification: **C12P 21/02**,  
C07K 1/36, 1/02, C12M 1/12, B04C 3/00

(21) International Application Number: PCT/PT01/00008

(22) International Filing Date: 17 May 2001 (17.05.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data: 102469 17 May 2000 (17.05.2000) PT

(71) Applicant (for all designated States except US): **INSTITUTO SUPERIOR TÉCNICO** [PT/PT]; Avenida Rovisco Pais, P-1049 001 Lisboa (PT).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **FRANÇA TEIXEIRA DOS PRAZERES, Duarte, Miguel** [PT/PT]; Rua da Penha de França, 234-C-3<sup>o</sup> Dr<sup>o</sup>, P. 1170 309 Lisboa (PT). **JORGE DIAS, Ana, Isabel** [PT/PT]; Avenida Rovisco

Pais, P-1049 001 Lisboa (PT). **FELICIANO SANTOS, Ana, Sofia** [PT/PT]; Avenida Rovisco Pais, P-1049 001 Lisboa (PT). **SAMPAIO CABRAL, Joaquim, Manuel** [PT/PT]; Rua Vila de Catió, Lote 397-1<sup>o</sup> Dr<sup>o</sup>, P-1800 348 Lisboa (PT). **MOURATO SERRALHEIRO, Maria, Luísa** [PT/PT]; Avenida Rovisco Pais, P-1049 001 Lisboa (PT).

(74) Agent: **CRUZ, João, Pereira da;** Rua Vitor Cordon, 14, P-1249 103 Lisboa (PT).

(81) Designated States (national): JP, US.

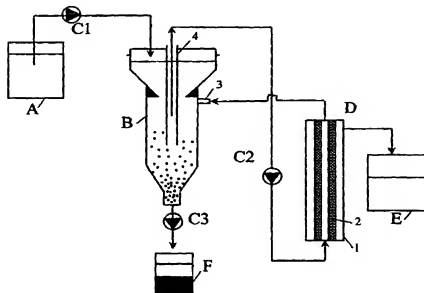
(84) Designated States (regional): European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR).

Published:

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: PROCESS FOR THE CONTINUOUS PRODUCTION OF DIPEPTIDE CRYSTALS IN A MEMBRANE AND HYDRO-CYCLONE REACTOR USING A PEPTIDASE



(57) Abstract: The invention relates to a process for the production of dipeptide crystals (generic formula  $\text{AcXYNH}_2$ ) with high purity (> 95 %), by enzymatic synthesis with a protease in organic media of reversed micelles, starting from derivatives of the two constituent amino acids ( $\text{AcXOEt}$  and  $\text{YNH}_2$ ). A membrane and hydro-cyclone reactor was designed which enables the continuous and simultaneous synthesis and crystallisation of the dipeptides. The dipeptide crystals thus prepared are continuously removed and further separated from the remaining liquid by filtration or centrifugation. After drying, the crystals are dissolved in hot methanol. By decreasing the temperature, the dipeptide re-crystallises, originating a high purity product. After re-crystallisation the product is filtered and dried.

WO 01/88175 A1